

Amendments to the Specification

Please replace paragraph [0007] with the following amended paragraph:

[0007] FIG. 1 is a side cross-sectional view of an embodiment of a device according to the present invention.

Please replace paragraph [0009] with the following amended paragraph:

[0009] FIG. 3 is a side cross-sectional view of an embodiment of a device according to the present invention.

Please replace paragraphs [0032]-[0033] with the following amended paragraphs:

[0032] Referring to FIG. 10, in another embodiment, the viscosity adjuster of system 80 is not a plunger but an expandable balloon 90. In order to apply force to reservoir 70, balloon 90 is expanded and contacted with reservoir 70. Although FIG. 9 depicts balloon 90 adjacent the proximal end of reservoir 70 [[50]], balloon 90 could be adjacent any surface of reservoir 70 [[50]] as long as balloon 90 is in a position to apply force to reservoir 70.

[0033] Although in the aforementioned embodiments, the viscosity adjuster is in the form of a plunger or balloon, the present invention contemplates any other form of the viscosity adjuster that can apply force to reservoir 70 [[50]] and thereby increase the shear stress in the non-Newtonian fluid contained therein resulting in an increase or decrease the viscosity of the non-Newtonian fluid (depending on whether the non-Newtonian fluid is a shear-thinning or shear-thickening fluid).

Please replace paragraphs [0037]-[0039] with the following amended paragraphs:

[0037] With respect to an exemplary use of a device according to the present invention, a non-Newtonian having therapeutic properties is loaded in channel 11 of a delivery device and urged through channel lumen 11c by any means known in the art. For example, a

syringe, a mechanical pump or a squeezable bladder may be used to urge the fluid through channel lumen 11c. The viscosity of the non-Newtonian fluid is adjusted by exposing the fluid to a viscosity adjuster of channel 11. The viscosity adjuster may comprise, for example, a configuration of channel 11 that increases the shear rate of the non-Newtonian fluid, an element that is adjustably positioned within channel 11 to increase the shear stress of the non-Newtonian fluid, or an element that is adjustably positioned within channel 11 to increase the shear rate of the non-Newtonian ~~Non-Newtonian~~ fluid. Depending on whether the non-Newtonian fluid is a shear-thinning or shear thickening fluid, the increase in shear rate or shear stress either increases or decreases the viscosity of the non-Newtonian fluid. The non-Newtonian fluid then exits the opening 13/60 of channel 11 (or reservoir 70) and is then delivered to the target site. After leaving the delivery device, the therapeutic is better suited to remain within the target site, particularly when the target site is actively contracting.

[0038] The non-Newtonian fluid having therapeutic properties may either act as a therapeutic itself or be loaded with a therapeutic. Non-limiting examples of therapeutics include pharmaceutically active compounds, proteins, cells, oligonucleotides, ribozymes, anti-sense oligonucleotides, DNA compacting agents, gene/vector systems (i.e., any vehicle that allows for the uptake and expression of nucleic acids), nucleic acids (including, for example, recombinant nucleic acids; dsRNA, naked DNA, cDNA, RNA; genomic DNA, cDNA or RNA in a non-infectious vector or in a viral vector and which further may have attached peptide targeting sequences; antisense nucleic acid (RNA or DNA); and DNA chimeras which include gene sequences and encoding for ferry proteins such as membrane translocating sequences ("MTS") and herpes simplex virus-1 ("VP22")), and viral, liposomes and cationic and anionic polymers and neutral polymers that are selected from a number of types depending on the desired application. Non-limiting examples of virus vectors or vectors derived from viral sources include adenoviral vectors, herpes simplex vectors, papilloma vectors, adeno-associated vectors, retroviral vectors, and the like. Non-limiting examples of biologically active solutes

include anti-thrombogenic agents such as heparin, heparin derivatives, urokinase, and PPACK (dextrophenylalanine proline arginine chloromethylketone); antioxidants such as probucol and retinoic acid; enzymes such as heme oxygenase that produce anti-oxidants and have anti-inflammatory, vasodilatory, and anti-proliferative action; angiogenic and anti-angiogenic agents and factors; agents blocking smooth muscle cell proliferation such as rapamycin, angiopeptin, and monoclonal antibodies capable of blocking smooth muscle cell proliferation; anti-inflammatory agents such as dexamethasone, prednisolone, corticosterone, budesonide, estrogen, sulfasalazine, acetyl salicylic acid, and mesalamine; calcium entry blockers such as verapamil, diltiazem and nifedipine; antineoplastic/antiproliferative/anti-mitotic agents such as paclitaxel, 5-fluorouracil, methotrexate, doxorubicin, daunorubicin, cyclosporine, cisplatin, vinblastine, vincristine, epothilones, endostatin, angiostatin, hKIS, and thymidine kinase inhibitors; antimicrobials such as triclosan, cephalosporins, aminoglycosides, and nitrofurantoin; ~~nitrofurantoin~~; anesthetic agents such as lidocaine, bupivacaine, and ropivacaine; nitric oxide (NO) donors such as linsidomine, ~~lisidomine~~, molsidomine, L-arginine, NO-protein adducts, NO-carbohydrate adducts, polymeric or oligomeric NO adducts; anti-coagulants such as D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, antithrombin compounds, platelet receptor antagonists, anti-thrombin antibodies, anti-platelet receptor antibodies, enoxaparin, hirudin, ~~Warafin~~ warfarin sodium, dicumarol ~~Dicumarol~~, aspirin, prostaglandin inhibitors, platelet inhibitors and tick antiplatelet factors; vascular cell growth promoters ~~promoters~~ such as growth factors, growth factor receptor antagonists, transcriptional activators, and translational promoters; vascular cell growth inhibitors such as growth factor inhibitors, growth factor receptor antagonists, transcriptional repressors, translational repressors, replication inhibitors, inhibitory antibodies, antibodies directed against growth factors, bifunctional molecules consisting of a growth factor and a cytotoxin, bifunctional molecules consisting of an antibody and a cytotoxin; cholesterol-lowering agents; vasodilating agents; agents which interfere with ~~endogenous vasoactive~~ endogenous vasoactive mechanisms; survival genes which protect against cell death, such as anti-apoptotic Bcl-2 family factors and

Akt kinase; and combinations thereof. Cells can be of human origin (autologous or allogenic) or from an animal source (xenogeneic), genetically engineered if desired to deliver proteins of interest at the injection site. The delivery mediated is formulated as needed to maintain cell function and viability. Any modifications are routinely made by one skilled in the art.

[0039] Polynucleotide sequences useful in practice of the invention include DNA or RNA sequences having a therapeutic effect after being taken up by a cell. Examples of therapeutic polynucleotides include anti-sense DNA and RNA; DNA coding for an anti-sense RNA; or DNA coding for tRNA or rRNA to replace defective or deficient endogenous molecules. The polynucleotides of the invention can also code for therapeutic proteins or polypeptides. A polypeptide is understood to be any translation product of a polynucleotide regardless of size, and whether glycosylated or not. Therapeutic proteins and polypeptides include as a primary example, those proteins or polypeptides that can compensate for defective or deficient species in an animal, or those that act through toxic effects to limit or remove harmful cells from the body. In addition, the polypeptides or proteins that can be injected, or whose DNA can be incorporated, include without limitation, bone marrow derived extracellular matrix, in vivo bioengineered extracellular matrix, angiogenic factors and other molecules competent to induce angiogenesis, including acidic and basic fibroblast growth factors, vascular endothelial growth factor, hif-1, epidermal growth factor, transforming growth factor α [[a]] and β , platelet-derived endothelial growth factor, platelet-derived growth factor, tumor necrosis factor α , hepatocyte growth factor and insulin like growth factor; growth factors; cell cycle inhibitors including CDK inhibitors; anti-restenosis agents, including p15, p16, p18, p19, p21, p27, p53, p57, Rb, nFkB and E2F decoys, thymidine kinase ("TK"), cladribine, and combinations thereof and other agents useful for interfering with cell proliferation, including agents for treating malignancies; and combinations thereof. Still other useful factors, which can be provided as polypeptides or as DNA encoding these polypeptides, include monocyte chemoattractant protein ("MCP-1"), the family of

tissue inhibitors of metalloproteinase ("TIMP"), and the family of bone morphogenic proteins (~~"BMP's"~~) ("BMPs"). The known proteins include BMP-2, BMP-3, BMP-4, BMP-5, BMP-6 (Vgr-1), BMP-7 (OP-1), BMP-8, BMP-9, BMP-10, BMP-11, BMP-12, BMP-13, BMP-14, BMP-15, and BMP-16. Currently preferred BMPs ~~BMP's~~ are any of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6 and BMP-7. These dimeric proteins can be provided as homodimers, heterodimers, or combinations thereof, alone or together with other molecules. Alternatively or, in addition, molecules capable of inducing an upstream or downstream effect of a BMP can be provided. Such molecules include any of the "hedgehog" proteins, or the DNAs ~~DNA's~~ encoding them.